Attached hereto is a sheet titled, "Version With Markings to Show Changes Made" which depicts the changes made to the instant application by the current amendment.

Drawings

Applicants acknowledge the Examiner's remarks regarding drawing corrections. Applicants respectfully request that the requirements be held in abeyance until such time as a Notice of Allowance is issued. Figures 12, 14, 16, 17, and 20 will be corrected by the submission of amended formal drawings which will place them in concordance with the brief description. The errors in the brief description of Figure 19 have been corrected by the current amendment.

Rejections Under 35 U.S.C. §112, first paragraph – scope of enablement

Claims 1-23 stand rejected under 35 U.S.C. §112, first paragraph as lacking an enabling disclosure. The Office Action acknowledges that the specification is enabling for measuring the interaction of TNIK with Nck, and for measuring activation of the JNK pathway. However, the Office Action alleges that methods of screening for agents capable of binding or modulating the activity of any and all cell cycle proteins, or interfering with the binding of any and all cell cycle proteins to Nck, are not enabled. Applicants respectfully traverse.

Applicants have amended Claims 19-23. Claim 19 recites the use of a TNIK protein comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:9-15, which are the amino acid sequences of TNIK isoforms 2-8, respectively. Claims 20-23 recite the use of a TNIK protein comprising an amino acid sequence having at least about 95% identity to SEQ ID NO:34, which is the amino acid sequence of TNIK isoform 1. Claims 20-23 further characterize the TNIK protein used in the methods by its binding properties. Particularly, the claims recite "wherein said TNIK protein will bind to Traf2 or Nck".

New Claims 24 and 25 depend from amended Claim 22.

Applicants submit that the instant claims are enabled in full scope by the specification, and respectfully request withdrawal of the rejection and allowance of the claims.

Rejections Under 35 U.S.C. §112, first paragraph – written description

Claims 19-23 stand rejected under 35 U.S.C. §112, first paragraph, as lacking written description support in the specification. Applicants respectfully traverse.

Claims 19-23 have been amended as discussed above. Amended Claim 19 recites the use of TNIK proteins comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:9-15. Claim 19 finds written description support throughout the entirety of the specification, as well as in drawings 29-35.

Amended Claims 20-23 recite the use of TNIK proteins comprising an amino acid sequence having at least about 95% identity to the amino acid sequence set forth in SEQ ID NO:34. Claims 20-23 find written description support, for example, at page 11, lines 18-22.

New Claims 24 and 25 depend from amended Claim 22, and recite measuring JNK pathway activation and observing actin filament rearrangement, respectively. The ability of TNIK to activate the JNK pathway and effect actin rearrangement is depicted in Figures 13 and 19, respectively, and described at, for example, page 6, line 12-19 and page 7, lines 13-19, respectively. Further, methods of screening for agents capable of modulating the activity of TNIK are described, for example, at page 36, lines 1-8.

Applicants submit that the amended and new claims satisfy the written description requirements of 35 U.S.C. §112, first paragraph, and respectfully request withdrawal of the rejection and allowance of the claims.

Rejections Under 35 U.S.C. §112, second paragraph – indefinite

Claims 19-23 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite. Particularly, Claims 19-23 are rejected for use of the phrase "bioactive agent", and Claim 23 is further rejected for use of the phrase "plurality of cells". Applicants respectfully traverse.

Claims 19-23 recite the use of *candidate* bioactive agents in a method to identify a bioactive agent that can bind to, interfere with binding to, and/or modulate the activity of, TNIK protein. Applicants point out that the agents used in the screening methods are referred to as "candidate bioactive agents", and that the method provides for obtaining candidate bioactive agents that are verified in their ability to bind to, interfere with binding to, and/or modulate the activity of, TNIK protein. Applicants submit that the adjective "bioactive" is appropriate for referring to agents obtained by the claimed methods, which therefore have the ability to bind to, interfere with binding to, or modulate the activity of, TNIK protein. Further, Applicants submit that the modifier "candidate" is an appropriate term for describing agents prior to screening and the determination of activity.

With regard to the phrase "plurality of cells", the current amendment replaces the phrase with "population of cells" for the purpose of technical clarity. At page 38, lines 6-15, the specification describes a population of cells as being at least two cells, with at least about 10^3 being preferred, at least about 10^6 being particularly preferred, and at least about 10^8 to 10^9 being especially preferred.

Applicants submit that the meaning of the phrase "population of cells" interpreted in view of the instant specification would be clear to one of reasonable skill in the art.

Applicants submit that the current amendment places Claims 19-23 in condition satisfying the requirements of 35 U.S.C. §112, second paragraph, and respectfully request withdrawal of the rejection and allowance of the claims.

Rejections Under 35 U.S.C. §102

Claims 19 and 22 stand rejected under 35 U.S.C. §102(a) as being anticipated by Suzuki et al. Claims 19 and 22 stand further rejected under 35 U.S.C. §102(b) as being anticipated by Kitamura et al. Claims 19-22 stand rejected under 35 U.S.C. §102(b) as being anticipated by Rothe et al. Claims 19, 22 and 23 stand rejected under 35 U.S.C. §102(b) as being anticipated by Draetta et al. Applicants respectfully traverse.

Claims 19-22 have been amended as discussed above. Prior to amendment, Claims 19-22 were directed to methods of screening for agents that bind to, interfere with binding to, or modulate the activity of, a cell cycle protein. The standing rejections under 35 U.S.C. §102 are all based on prior art methods using cell cycle proteins which are distinct from the instant TNIK proteins.

Applicants point out that amended Claim 19 recites the use of a TNIK protein comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:9-15, while Claims 20-23 recite the use of a TNIK protein comprising an amino acid sequence having at least about 95% identity to SEQ ID NO:34. Claims 20-23 further characterize the TNIK protein used in the method by its binding properties, particularly the ability to bind to Traf2 or Nck, and Claims 24 and 25 depend from amended Claim 22.

Applicants submit that Suzuki et al., Kitamura et al., Rothe et al. and Draetta et al. teach methods involving the use of proteins distinct from the TNIK proteins recited in the instant claims. Accordingly, Applicants submit that the cited art does not teach each and every element recited in the instant claims, and that the instant claimed invention is not anticipated by the cited prior art. Applicants respectfully request withdrawal of the rejection and allowance of the claims.

CONCLUSIONS

Applicants submit that the application is now in condition for allowance, and early notification of such is requested. If there remain issues that the Examiner believes may be

resolved by telephone, he/she is respectfully requested to contact the undersigned at (415) 781-1989.

Respectfully submitted,
Dorsey & Whitney LLP

Dated 8/22/02

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Version With Markings to Show Changes Made

In the Specification:

Figure 19 shows a picture of a gel showing Tnik overexpression induced redistribution of actin. Phoenix-A cells were transfected with 3 μg of vector, HA-Tnik(WT) or HA-Tnik(KM) and lysed with 1% Triton X-100 as described in EXPERIMENTAL PROCEDURES. Top panel: Cell lysates (4 x 104 cells) from either Triton X-100 soluble (lanes 1-3) or insoluble (lanes 4-6) fractions were resolved on SDS-PAGE and immunoblotted with an anti-β-actin mAb. [~~Bottom panel: Total cell lysates were blotted with an anti-HA mAb to control for expression levels of Tnik(WT) and Tnik(KM).~~]

In the Claims:

19. (amended) A method [~~for~~] of screening for a bioactive agent capable of binding to a [~~cell cycle~~] TNIK protein, said method comprising:

a) combining a [~~cell cycle protein and a~~] candidate bioactive agent and a TNIK protein; and

b) determining the binding of said candidate bioactive agent to said [~~cell cycle~~] protein[~~.~~];

wherein said TNIK protein comprises an amino acid sequence selected from the group consisting of the amino acid sequences set forth by SEQ ID NOs:9-15.

20. (amended) A method [~~for~~] of screening for a bioactive agent capable of interfering with the binding of a [~~cell cycle~~] TNIK protein and a Traf2 or Nck protein, said method comprising:

a) combining a [~~cell cycle~~] TNIK protein, a candidate bioactive agent, and a Traf2 or Nck protein; and

b) determining the binding of said [~~cell cycle~~] TNIK protein [~~and~~] to said Traf2 or Nck protein[~~.~~];

wherein said TNIK protein comprises an amino acid sequence having at least about 95% identity to SEQ ID NO:34, and wherein said TNIK protein will bind to said Traf2 or Nck protein in the absence of said candidate bioactive agent.

21. (amended) [~~A~~] The method [~~according to Claim 20~~] of Claim 19, wherein said [~~cell cycle~~] TNIK protein and said Traf2 or Nck protein are combined first.

22. (amended) A method [~~for~~] of screening for a bioactive agent capable of modulating the activity of [cell cycle] a TNIK protein, said method comprising:

a) adding a candidate bioactive agent to a cell comprising a recombinant nucleic acid encoding a [~~cell cycle~~] TNIK protein; and

b) determining the effect of said candidate bioactive agent on said cell[.];

wherein said TNIK protein comprises an amino acid sequence having at least about 95% identity to SEQ ID NO:34, and wherein said TNIK protein will bind to Traf2 or Nck.

23. (amended) [~~A method according to~~] The method of Claim 22, wherein a library of candidate bioactive agents is added to a [~~plurality~~] population of cells comprising a recombinant nucleic acid encoding a [~~cell cycle~~] TNIK protein.

24. (new) The method of Claim 22, wherein determining the effect of said candidate bioactive agent on said cell involves measuring JNK pathway activation in said cell.

25. (new) The method of Claim 22, wherein determining the effect of said candidate bioactive agent on said cell involves observing actin filament rearrangement in said cell.